REMARKS

Status of the Claims.

Claims 51 and 60-68, 74, 75, and 293 are pending with entry of this amendment, claims 1-50, 52-59, 69-73, and 76-292 being canceled, and claim 293 being added herein. Claims 51 and 60-68, 74, 75 are amended herein. The amendments and new claim introduce no new matter. Support is replete throughout the specification (*e.g.,* at page 8, lines 13-15, page 11, lines 26-28, page 12, lines 8-19, and the like).

As a preliminary matter, Applicants acknowledge and appreciate the withdrawal of the previous rejections under 35 U.S.C. §112, first and second paragraph and the acceptance of the amendments to the figures and specification.

35 U.S.C. §102.

Claims 51 and 60-79 stand rejected under 35 U.S.C. §102(b) as being anticipated by "Hoppe et al., 1995, IDS" which Applicants understand to be Hoppe *et al.* (1995) *Upregulation of a 46 kDa Collagen Binding Protein Correlates With Protection of HUVEC Cells In Vitro Against Cytolysis By CD3+56+CTL and IL-2 Stimulated Natural Killer Cells, Blood,* 86 (Suppl 1) 322A (abstract 1277). Applicants traverse.

Independent claims 51, 60, and 66 are directed to the use of isolated or recombinantly expressed polypeptides. Thus, for example, claim 51 recites:

> 51. A method for reducing immune-mediated damage to cells, tissues or organs comprising contacting a cell, tissue or organ with an immunoprotective amount of **an isolated or recombinantly expressed polypeptide** comprising the amino acid sequence AVLSAEQLR (SEQ ID NO:3), wherein the immune-mediated damage is caused by lymphocytes, NK cells or NK-like cells. [emphasis added]

In contrast, Hoppe *et al.* describes the treatment of HUVEC cells with Brefeldin A (BFA) which induced cell membrane expression of a 46 kD glycoprotein (p46). The abstract further states that "p46 **may** represent a human form of gp46 also described as heat shock protein 47 (Hsp47) or colligin.

The reference thus teaches that BFA is associated with the upregulation of an **endogenous** protein. **The reference offers no disclosure or teaching regarding the administration**

of an isolated or recombinantly expressed polypeptide. Moreover, the reference fails to establish that p46 is actually the HSP47 protein referenced in the presently pending claims. For these reasons, among others, Hoppe *et al.* fails to teach or disclose all the elements of the presently pending claims. Accordingly, the rejection of claims 51 and 60-79 under 35 U.S.C. §102(b) should be withdrawn.

35 U.S.C. §112, First Paragraph.

Claims 60-79 were rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the enablement requirement. In particular, the Examiner alleged that the specification is not enabling for any polypeptides other than those of SEQ ID NOS: 3 and 6. Applicants traverse.

The Examiner is reminded that to be enabling under §112, first paragraph, a patent must contain a description that enables one skilled in the art to make and use the claimed invention. **That some experimentation is necessary does not constitute a lack of enablement**; the amount of experimentation, however, must not be unduly extensive. *Hybritech Inc, V. Monoclonal Antibodies, Inc.,* 802 F.2d 1367, 1384, 231 U.S.P.Q. 81, 94 (Fed. Cir. 1986).

Whether undue experimentation is required by one skilled in the art is typically determined by reference to eight factors considered relevant to the inquiry: (1) quantity of experimentation necessary; (2) amount of guidance presented; (3) presence of working examples; (4) nature of the invention; (5) state of the prior art; (6) relative skill of those in the art; (7) predictability of the art; and (8) breadth of the claims. *In re Wands,* 8 USPQ2d 1400 (Fed. Cir. 1988) *citing Ex parte Forman Inc.,* 230 USPQ 546 (BPAI 1986).

Moreover, the Examiner is also reminded that a claim need not exclude possible inoperable embodiments. As stated by the PTO Board of Appeals:

> It is always possible to theorize some combination of circumstances which would render a claimed composition or method inoperative, but the art-skilled would assuredly not choose such a combination. *Ex parte* Cole, 223 USPQ 94 (BPAI 1983)

For a proposed claim to be unpatentable, the law requires that the number of inoperable embodiments be significant in numbers **and not readily ascertained** by those of skill. *In re Cook and Merigold*, 169 USPQ 298, 301-302 (CCPA, 1971).

In the present case **inoperable embodiments are readily ascertained** by one of ordinary skill in the art and are **expressly excluded** by the claims, which as amended herein recite that the peptide **has the immunoprotective properties of the polypeptide presented as SEQ ID NO:6.**

Applicants have amended the claims herein to recite methods for protecting cells, organs or tissues comprising exposing the cells, organs or tissues to an immunoprotective amount of a polypeptide comprising the amino acid sequence presented as SEQ ID NO:3 or SEQ ID NO:6 or a polypeptide having substantial sequence identity to the amino acid sequence presented as SEQ ID NO:3 or SEQ ID NO:6 and the immunoprotective properties of the polypeptide presented as SEQ ID NO:6. The current claims are thus consistent in scope with the disclosure, given that the claims require the polypeptide employed in the method exhibit the immunoprotective properties of the polypeptide presented as SEQ ID NO:6.

With respect to the substantially similar peptides having immunoprotective properties, it is known in the art how to make substitutions within a polypeptide sequence. The specification teaches calculation of sequence identity of one sequence to another, and the specification teaches how to screen the peptide(s) for immonoprotective properties. In addition, the Federal Circuit, in *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988) expressly held that **it was not undue experimentation to screen large numbers of hybridomas for particular desired monoclonal antibodies**. Similarly, in the present case, it is not undue experimentation to screen peptides having the recited sequence identity for immunoprotective activity.

Specifically, with respect to the factors recited in *Wands,* Applicants note that relatively little experimentation is necessary (simply producing and screening polypeptides having the desired sequence identity) and the Federal Circuit has determined that routine screening is not undue experimentation (Wands Factor 1). The specification provides ample guidance, *e.g.* as put forth in Figure 2 (Wands Factor 2). Working examples (Wands Factor 3) are provided. The prior art is well developed in this area (Wands Factor 4). The level of skill in the art is high (Ph.D./M.D.). Utilizing the teaching provided in the specification, the predictability of the art is high (Wands Factor 7), and the claims are relatively narrow being directed to the use of two peptides or other peptides having a high degree of sequence identity and similar immunoprotective activity.

In view of the foregoing, undue experimentation is simply not required to practice the presently claimed invention. Accordingly, the rejection under 35 U.S.C. §112, first paragraph, should be withdrawn.

35 U.S.C. §112, First Paragraph, Written Description.

Claims 70-72 and 74-77 were rejected under 35 U.S.C. §112, first paragraph, as allegedly failing to meet the written description requirement. Applicants traverse.

The Patent Office guidelines state that the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus.

Description of a representative number of species does not require the description to be of such specificity that it would provide individual support for each species that the genus embraces. Indeed, as set forth in the MPEP: a patent need not teach, and preferably omits, what is well known in the art. *In re Buchner,* 929 F.2d 660, 661, 18 USPQ2d 1331, 1332 (Fed. Cir. 1991); *Hybritech, Inc. v. Monoclonal Antibodies , Inc .,* 802 F.2d 1367, 1384, 231 USPQ 81, 94 (Fed. Cir. 1986), *cert. denied,* 480 U.S. 947 (1987); and *Lindemann Maschinenfabrik GMBH v. American Hoist & Derrick Co.,* 730 F.2d 1452, 1463, 221 USPQ 481, 489 (Fed. Cir. 1984).

Claims 70-72, and 76-77 have been cancelled and pending claims 74 and 75 have been amended to clarify that the claimed methods rely on polypeptides that comprise the AVLSAEQLR sequence, and that exhibit the immunoprotective properties of SEQ ID NO:6. The claims also make reference to sequences have specific percentage identity with the HSP47 sequence. Support for this claim language is provided at least on page 10, lines 3-12 and page 12, lines 1-15.

In view of the specific examples and general guidance provided by Applicants, one of skill in the art could readily determine that the Applicant was in possession of the claimed sequences at the time the application was filed. Withdrawal of the written description rejection is respectfully requested.

In view of the foregoing, Applicants believe all claims now pending in this application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested. Should the Examiner seek to maintain the rejections, Applicants request a telephone interview with the Examiner and the Examiner's supervisor.

If a telephone conference would expedite prosecution of this application, the Examiner is invited to telephone the undersigned at (510) 267-4161.

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Respectfully submitted,

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